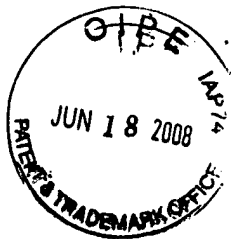


The instant application is a national stage application of a PCT international application and thus unity of invention practice is applicable (see, e.g., MPEP § 1893.03(d)). Accordingly, a restriction requirement is proper if and only if the national stage application lacks unity of invention (see, e.g., 37 C.F.R. § 1.499). Unity of invention practice is set forth in PCT Rules 13.1 and 13.2. Under Rule 13.1 an international application can include more than one invention provided the inventions are so linked as to form a single general inventive concept. Under Rule 13.2 a single general inventive concept exists when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. The term "special technical features" refers to the technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. It is well recognized that combinations of claims of different categories can be included in the same application. In the instant application, claims 1-12 and 19 of Group I relate to a compound of Formula I, and claims 13 and 14 of Group II relate to a use of a compound of Formula I. There is unity between Groups I and II wherein a compound of Formula I is the special technical feature common to both groups. The circumstance in this application is analogous to that set forth in section (e)(i) of Annex B in Appendix AI of the MPEP, which states that unity of invention permits the combination of a claim for a given product and a claim for a use of said product. Withdrawal of the restriction requirement is requested.

Respectfully submitted,

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Date: June 16, 2008



IAP6 Rec'd PCT/PTO 08 SEP 2006

THE PATENT & TRADEMARK OFFICE ACKNOWLEDGES, AND HAS STAMPED HEREON, THE DATE OF
THE RECEIPT AND THE ASSIGNED SERIAL NUMBER OF THE FOLLOWING PATENT APPLICATION:

CASE NUMBER 21548YP	DATE 09/08/06	ATTORNEY K. R. Walton	EXPRESS MAIL <input checked="" type="checkbox"/> EV660601936US
TITLE HIV INTEGRASE INHIBITORS			
INVENTORS Matthew M. Morrisette, Peter D. Williams, John S. Wai, Thorsten E. Fisher and Terry A. Lyle			
NO. OF PAGES 87	NO. OF CLAIMS 15	PAGES OF DRAWINGS N/A	SEQUENCE LISTING N/A
DECLARATIONS - Copy Enclosed Information Disclosure Statement w/ Ref's Preliminary Amendment		ACCOUNT CHARGE 13-2755 \$300.00	

10/591914



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Morrisette et al.

Serial No.: Not Yet Assigned (U.S. National Phase Application of
International Application No. PCT/US2005/007106, filed
March 4, 2005)

Docket No.: 21548YP

Mailed: September 8, 2006 (Express Mail)

For: HIV INTEGRASE INHIBITORS

Art Unit:

Not Yet Assigned

Examiner:

Not Yet Assigned

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

PRELIMINARY AMENDMENT

Sir:

Applicants request entry of this amendment prior to examination of the above-identified application. Please amend the above-identified application as follows:

An amendment to the specification is shown on page 2 of this paper.

Amendments to the claims are shown in the listing of the claims that begins on page 3 of this paper.

Remarks begin on page 16 of this paper.

EXPRESS MAIL CERTIFICATE
DATE OF DEPOSIT Sept. 8 2006
EXPRESS MAIL NO. 9516000193645
I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS
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ALEXANDRIA, VIRGINIA 22313-1450.
MAILED BY Martin Cuffe
DATE 9-8-06

Amendments to the Specification

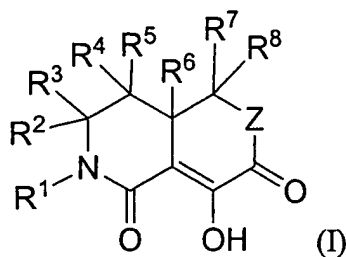
Replace the paragraph following the title of the invention on page 1 with the following rewritten paragraph:

-- This application is the National Stage of International Application No. PCT/US2005/007106, filed on March 4, 2005, which claims the benefit of U.S. Provisional Application No. 60/551,440, filed March 9, 2004, the disclosure of which is hereby incorporated by reference in its entirety.--

IN THE CLAIMS

The listing of the claims which follows replaces any and all prior versions and/or listings of the claims in the application.

1. (currently amended) A compound of Formula I, or an individual ~~optical~~ ~~isomer~~ enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof:



wherein:

Z is O or N-R⁹;

R¹ is -C₁₋₆ alkyl substituted with R^J, wherein R^J is:

(A) aryl or aryl fused to a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, wherein the aryl or fused aryl is

(i) optionally substituted with from 1 to 5 substituents each of which is independently:

- (1) -C₁₋₆ alkyl, which is optionally substituted with -OH, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -CN, -NO₂, -N(RA)RB, -C(=O)N(RA)RB, -C(=O)RA, -CO₂RA, -S(O)_nRA, -SO₂N(RA)RB, -N(RA)C(=O)RB, -N(RA)CO₂RB, -N(RA)SO₂RB, -N(RA)SO₂N(RA)RB, -OC(=O)N(RA)RB, or -N(RA)C(=O)N(RA)RB,
- (2) -O-C₁₋₆ alkyl,
- (3) -C₁₋₆ haloalkyl,
- (4) -O-C₁₋₆ haloalkyl,
- (5) -OH,
- (6) halo,
- (7) -CN,
- (8) -NO₂,
- (9) -N(RA)RB,

- (10) $-C(=O)N(RA)RB$,
- (11) $-C(=O)RA$,
- (12) $-CO_2RA$,
- (13) $-SRA$,
- (14) $-S(=O)RA$,
- (15) $-SO_2RA$,
- (16) $-SO_2N(RA)RB$,
- (17) $-N(RA)SO_2RB$,
- (18) $-N(RA)SO_2N(RA)RB$,
- (19) $-N(RA)C(=O)RB$,
- (20) $-N(RA)C(=O)-C(=O)N(RA)RB$, or
- (21) $-N(RA)CO_2RB$, and

(ii) optionally substituted with 1 or 2 substituents each of which is independently:

- (1) aryl,
- (2) $-C_{1-6}$ alkyl substituted with aryl,
- (3) $-HetA$,
- (4) $-C(=O)-HetA$; or
- (5) $-HetB$;

wherein each $HetA$ is independently a C_{4-7} azacycloalkyl or a C_{3-6} diazacycloalkyl, either of which is optionally substituted with from 1 to 3 substituents each of which is independently oxo or C_{1-6} alkyl; and

wherein each $HetB$ is a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, wherein the heteroaromatic ring is optionally substituted with from 1 to 4 substituents each of which is independently halo, $-C_{1-6}$ alkyl, $-C_{1-6}$ haloalkyl, $-O-C_{1-6}$ alkyl, $-O-C_{1-6}$ haloalkyl, or hydroxy; or

- (B) a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; wherein the heteroaromatic ring is:
- (i) optionally substituted with from 1 to 4 substituents each of which is independently halogen, $-C_{1-6}$ alkyl, $-C_{1-6}$ haloalkyl, $-O-C_{1-6}$ alkyl, $-O-C_{1-6}$ haloalkyl, or hydroxy, and
 - (ii) optionally substituted with 1 or 2 substituents each of which is independently aryl or $-C_{1-6}$ alkyl substituted with aryl;

R², R³, R⁴ and R⁵ are defined as follows:

- (A) R², R³, R⁴ and R⁵ are each independently:
- (1) -H,
 - (2) -C₁₋₆ alkyl, which is optionally substituted with -OH, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -CN, -N(RA)RB, -C(=O)N(RA)RB, -C(=O)RA, -CO₂RA, -S(O)_nRA, -SO₂N(RA)RB, -N(RA)C(=O)RB, -N(RA)CO₂RB, -N(RA)SO₂RB, -N(RA)SO₂N(RA)RB, -N(RA)C(=O)N(RA)RB, or -OC(=O)N(RA)RB,
 - (3) -C₁₋₆ haloalkyl,
 - (4) CycA,
 - (5) AryA,
 - (6) HetC, or
 - (7) -C₁₋₆ alkyl substituted with CycA, AryA, or HetC;
- (B) R² and R⁴ together with the carbon atoms to which each is attached form a carbon-carbon double bond; and R³ and R⁵ are each independently as defined in part A above;
- (C) R² and R³ together with the carbon atom to which they are both attached form a 3- to 8-membered saturated carbocyclic ring which is optionally substituted with from 1 to 4 substituents each of which is independently -OH, -C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ alkyl, or -O-C₁₋₆ haloalkyl; and R⁴ and R⁵ are each independently as defined in part A above; or
- (D) R⁴ and R⁵ together with the carbon atom to which they are both attached form a 3- to 8-membered saturated carbocyclic ring which is optionally substituted with from 1 to 4 substituents each of which is independently -OH, -C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ alkyl, or -O-C₁₋₆ haloalkyl; and R² and R³ are each independently as defined in part A above;

R⁶ is:

- (1) -H,
- (2) -C₁₋₆ alkyl, which is optionally substituted with -OH, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -CN, -N(RA)RB, -C(=O)N(RA)RB, -C(=O)RA, -CO₂RA, -S(O)_nRA, -SO₂N(RA)RB, -N(RA)C(=O)RB, -N(RA)CO₂RB, -N(RA)SO₂RB, -N(RA)SO₂N(RA)RB, -N(RA)C(=O)N(RA)RB, or -OC(=O)N(RA)RB,
- (3) -C₁₋₆ haloalkyl,
- (4) CycA,

- (5) AryA,
- (6) HetC, or
- (7) -C₁₋₆ alkyl substituted with CycA, AryA, or HetC;

R⁷ and R⁸ are each independently:

- (1) -H,
- (2) -C₁₋₆ alkyl, which is optionally substituted with -OH, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -CN, -N(RA)RB, -C(=O)N(RA)RB, -C(=O)RA, -CO₂RA, -S(O)_nRA, -SO₂N(RA)RB, -N(RA)C(=O)RB, -N(RA)CO₂RB, -N(RA)SO₂RB, -N(RA)SO₂N(RA)RB, -N(RA)C(=O)N(RA)RB, or -OC(=O)N(RA)RB,
- (3) -C₁₋₆ haloalkyl,
- (4) -C(=O)RA,
- (5) -CO₂RA,
- (6) -C(=O)N(RA)RB,
- (7) -N(RA)SO₂N(RA)RB,
- (8) -RK,
- (9) -C(=O)-RK,
- (10) -C(=O)N(RA)-RK,
- (11) -C(=O)N(RA)-C₁₋₆ alkylene-RK, or
- (12) -C₁₋₆ alkyl substituted with -RK, -C(=O)-RK, -C(=O)N(RA)-RK, or -C(=O)N(RA)-C₁₋₆ alkylene-RK;

or alternatively R⁷ and R⁸ together with the carbon atom to which they are both attached form a 3- to 8-membered saturated carbocyclic ring which is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ alkyl, or -O-C₁₋₆ haloalkyl;

R⁹ is:

- (1) -H,
- (2) -C₁₋₆ alkyl, which is optionally substituted with -OH, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -CN, -N(RA)RB, -C(=O)N(RA)RB, -C(=O)RA, -CO₂RA, -S(O)_nRA, -SO₂N(RA)RB, -N(RA)C(=O)RB, -N(RA)CO₂RB, -N(RA)SO₂RB, -N(RA)SO₂N(RA)RB, -N(RA)C(=O)N(RA)RB, or -OC(=O)N(RA)RB,
- (3) -C₁₋₆ haloalkyl,
- (4) CycA,
- (5) AryA,

- (6) HetC, or
- (7) -C₁₋₆ alkyl substituted with CycA, AryA, or HetC;

each n is independently an integer equal to zero, 1, or 2;

each R^A is independently H or C₁₋₆ alkyl;

each R^B is independently H or C₁₋₆ alkyl;

each R^K is independently CycA, AryA, or HetC;

each CycA is independently a C₃₋₈ cycloalkyl, which is optionally substituted with from 1 to 4 substituents each of which is halogen, -OH, -C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ alkyl, or -O-C₁₋₆ haloalkyl;

each AryA is independently an aryl, which is

- (a) optionally substituted with from 1 to 5 substituents each of which is independently -C₁₋₆ alkyl, -C₁₋₆ alkylene-OH, -C₁₋₆ alkylene-O-C₁₋₆ alkyl, -C₁₋₆ alkylene-O-C₁₋₆ haloalkyl, -C₁₋₆ alkylene-N(R^A)R^B, -C₁₋₆ alkylene-C(=O)N(R^A)R^B, -C₁₋₆ alkylene-C(=O)R^A, -C₁₋₆ alkylene-CO₂R^A, -C₁₋₆ alkylene-S(O)_nR^A, -O-C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ haloalkyl, -OH, halo, -N(R^A)R^B, -C(=O)N(R^A)R^B, -C(=O)R^A, -CO₂R^A, -S(O)_nR^A, or -SO₂N(R^A)R^B, and
- (b) optionally substituted with C₃₋₈ cycloalkyl, aryl, HetD, or -C₁₋₆ alkyl substituted with C₃₋₈ cycloalkyl, aryl, or HetD;

each HetC is independently a 4- to 7-membered saturated or unsaturated heterocyclic ring containing at least one carbon atom and from 1 to 4 heteroatoms independently selected from N, O and S, wherein the heterocyclic ring is

- (a) optionally substituted with from 1 to 4 substituents each of which is halogen, -C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, OH, or oxo, and
- (b) optionally substituted with C₃₋₈ cycloalkyl, aryl, HetD, or -C₁₋₆ alkyl substituted with C₃₋₈ cycloalkyl, aryl, or HetD;

each HetD is independently a 4- to 7-membered saturated or unsaturated heterocyclic ring containing at least one carbon atom and from 1 to 4 heteroatoms independently selected from N, O and S; and

each aryl is independently (i) phenyl or (ii) a 9- or 10-membered bicyclic, fused carbocyclic ring system in which at least one ring is aromatic.

2. (original) The compound according to claim 1, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, wherein Z is N-R⁹.

3. (original) The compound according to claim 1, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, wherein R¹ is -CH₂-R^J, and R^J is phenyl, pyridyl, quinoliny, isoquinoliny, cinnoliny, or quinazoliny, any of which is

(a) optionally substituted with from 1 to 4 substituents each of which is independently:

- (1) -C₁₋₄ alkyl,
- (2) -O-C₁₋₄ alkyl,
- (3) -C₁₋₄ haloalkyl,
- (4) -O-C₁₋₄ haloalkyl,
- (5) halo,
- (6) -CN,
- (7) -N(R^A)R^B,
- (8) -C(=O)N(R^A)R^B,
- (9) -S(=O)R^A,
- (10) -SO₂R^A,
- (11) -N(R^A)SO₂R^B,
- (12) -N(R^A)SO₂N(R^A)R^B,
- (13) -N(R^A)C(=O)R^B, or
- (14) -N(R^A)C(=O)-C(=O)N(R^A)R^B, and

(b) optionally substituted with phenyl, benzyl, -HetA, or -C(=O)-HetA; wherein each HetA is independently a C₄₋₇ azacycloalkyl or a C₃₋₆ diazacycloalkyl, either of which is optionally substituted with from 1 to 3 substituents each of which is independently oxo or C₁₋₄ alkyl; and with the proviso that when HetA is attached

to the rest of the compound via the -C(=O)- moiety, the HetA is attached to the -C(=O)- via a ring N atom.

4. (original) The compound according to claim 1, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, wherein R², R³, R⁴ and R⁵ are defined as follows:

- (A) R² and R⁴ are as defined in part A of claim 1, and R³ and R⁵ are both H;
- (B) R² and R⁴ are as defined in part B of claim 1; and R³ and R⁵ are both H;
- (C) R² and R³ are as defined in part C of claim 1; and R⁴ and R⁵ are both H; or
- (D) R⁴ and R⁵ are as defined in part D of claim 1; and R² and R³ are both H.

5. (original) The compound according to claim 1, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, wherein R⁶ is:

- (1) -H,
- (2) -C₁₋₆ alkyl,
- (3) -C₁₋₆ fluoroalkyl,
- (4) CycA,
- (5) AryA, or
- (6) -C₁₋₆ alkyl substituted with AryA.

6. (original) The compound according to claim 5, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, wherein R⁶ is H.

7. (original) The compound according to claim 1, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, wherein R⁷ and R⁸ are each independently:

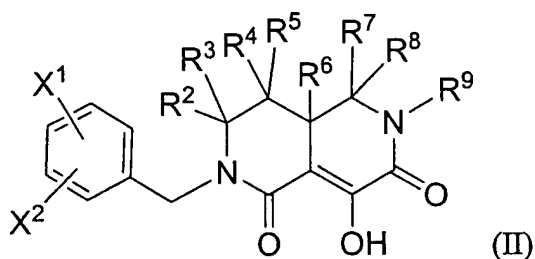
- (1) -H,
- (2) -C₁₋₆ alkyl,
- (3) -CO₂RA,
- (4) -C(=O)N(RA)RB,
- (5) -RK,
- (6) -C(=O)-RK,
- (7) -C(=O)N(RA)-RK, or
- (8) -C(=O)N(RA)-C₁₋₆ alkylene-RK;

or alternatively R⁷ and R⁸ together with the carbon atom to which they are both attached form a 3- to 7-membered saturated carbocyclic ring.

8. (original) The compound according to claim 1, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, wherein R⁹ is:

- (1) -H,
- (2) -C₁₋₆ alkyl
- (3) -C₁₋₆ fluoroalkyl,
- (4) CycA, or
- (5) -C₁₋₆ alkyl substituted with CycA, AryA, or HetC.

9. (original) A compound of Formula II, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof:



wherein:

X¹ and X² are each independently -H, -C₁₋₄ alkyl, -O-C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ haloalkyl, halo, -CN, -N(RA)RB, -C(=O)N(RA)RB, or -S(O)_nRA, wherein n is an integer equal to zero, 1, or 2;

R², R³, R⁴ and R⁵ are defined as follows:

- (A) R² and R⁴ are each independently -H, -C₁₋₄ alkyl, -C₁₋₄ fluoroalkyl, C₃₋₆ cycloalkyl, phenyl, or benzyl; and R⁴ and R⁵ are both H;
- (B) R² and R⁴ together with the carbon atoms to which each is attached form a carbon-carbon double bond; and R³ and R⁵ are both H;
- (C) R² and R³ together with the carbon atom to which they are both attached form cyclopropyl; and R⁴ and R⁵ are both H; or
- (D) R⁴ and R⁵ together with the carbon atom to which they are both attached form cyclopropyl; and R² and R³ are both H;

R⁶ is H, -C₁₋₄ alkyl, CF₃, cyclopropyl, phenyl or benzyl;

R⁷ is H or -C₁₋₄ alkyl;

R⁸ is -H, -C₁₋₄ alkyl, -CO₂-C₁₋₄ alkyl, -C(=O)NH(C₁₋₄ alkyl), -C(=O)N(C₁₋₄ alkyl)₂, C₃₋₆ cycloalkyl, HetF, -C(=O)-HetE, or -C(=O)N(R^A)-(CH₂)₁₋₂-HetF; wherein

HetE is a 4- to 7-membered saturated heterocyclic ring containing at least one carbon atom and from 1 to 4 heteroatoms selected from 1 to 4 N atoms, zero or 1 oxygen atom, and zero or 1 sulfur atom, wherein the saturated heterocyclic is optionally substituted with from 1 to 3 substituents each of which is independently oxo or C₁₋₄ alkyl; and with the proviso that the saturated heterocyclic is attached to the -C(=O)- via a ring N atom; and

HetF is a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, wherein the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently a C₁₋₄ alkyl;

or alternatively R⁷ and R⁸ together with the carbon atom to which they are both attached form a 3- to 6-membered saturated carbocyclic ring;

R⁹ is -H, -C₁₋₄ alkyl, -CH₂CF₃, -C₃₋₆ cycloalkyl, -CH₂-C₃₋₆ cycloalkyl, or -CH₂-phenyl;

each R^A is independently H or C₁₋₄ alkyl; and

each R^B is independently H or C₁₋₄ alkyl.

10. (original) A compound according to claim 9, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, wherein:

X¹ and X² are each independently H, fluoro, chloro, methyl, trifluoromethyl, methoxy, CN, -SO₂CH₃, -C(=O)NH(CH₃), or -C(=O)N(CH₃)₂;

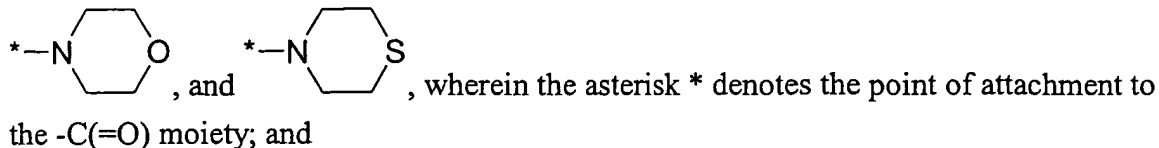
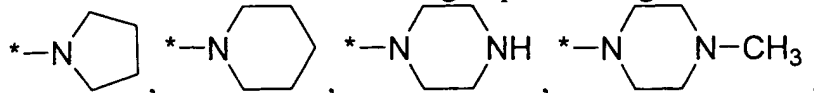
R², R³, R⁴ and R⁵ are all H;

R⁶ is H, methyl, cyclopropyl, or phenyl;

R⁷ is H or methyl;

R⁸ is -H, -C₁₋₄ alkyl, -CO₂-C₁₋₄ alkyl, -C(=O)NH(C₁₋₄ alkyl), -C(=O)N(C₁₋₄ alkyl)₂, C₃₋₆ cycloalkyl, HetF, -C(=O)-HetE, or -C(=O)N(R^A)-(CH₂)₁₋₂-HetF; wherein

HetE is selected from the group consisting of:



HetF is selected from the group consisting of pyrrolyl, imidazolyl, triazolyl, tetrazolyl, oxazolyl, isooxazolyl, pyridyl, pyrimidinyl, and pyrazinyl;

or alternatively R⁷ and R⁸ together with the carbon atom to which they are both attached form cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl; and

R⁹ is H, methyl, ethyl, n-propyl, isopropyl, -CH₂CF₃, cyclopropyl, or -CH₂-cyclopropyl.

11. (original) A compound, or a pharmaceutically acceptable salt thereof, selected from the group consisting of:

2-(4-fluorobenzyl)-8-hydroxy-6-methyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

2-(4-fluorobenzyl)-8-hydroxy-5,5,6-trimethyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

(+)-2-(4-fluorobenzyl)-8-hydroxy-5,5,6-trimethyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

(-)-2-(4-fluorobenzyl)-8-hydroxy-5,5,6-trimethyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

2-(4-fluorobenzyl)-8-hydroxy-6-methyl-4a-phenyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

(+)-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-4a-phenyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

(-)-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-4a-phenyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

5-(tert-butyloxycarbonyl)-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione, and diastereomers and enantiomers thereof;

5-ethyl-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione, and diastereomers and enantiomers thereof;

6-(cyclopropylmethyl)-2-(4-fluorobenzyl)-8-hydroxy-5,5-dimethyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

5-(dimethylaminocarbonyl)-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione, and diastereomers and enantiomers thereof

2-(3-chloro-4-fluorobenzyl)-8-hydroxy-5,5,6-trimethyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

(+)-2-(3-chloro-4-fluorobenzyl)-8-hydroxy-5,5,6-trimethyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

(-)-2-(3-chloro-4-fluorobenzyl)-8-hydroxy-5,5,6-trimethyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

6'-(4-fluorobenzyl)-4'-hydroxy-2'-methyl-6',7',8',8a'-tetrahydro-2' *H*-spiro[cyclopentane-1,1'-[2,6]naphthyridine]-3',5'-dione;

(+)-6'-(4-fluorobenzyl)-4'-hydroxy-2'-methyl-6',7',8',8a'-tetrahydro-2' *H*-spiro[cyclopentane-1,1'-[2,6]naphthyridine]-3',5'-dione;

(-)-6'-(4-fluorobenzyl)-4'-hydroxy-2'-methyl-6',7',8',8a'-tetrahydro-2' *H*-spiro[cyclopentane-1,1'-[2,6]naphthyridine]-3',5'-dione;

2-(3,4-difluorobenzyl)-8-hydroxy-5,5,6-trimethyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

6'-(4-fluorobenzyl)-4'-hydroxy-2'-methyl-6',7',8',8a'-tetrahydro-2' *H*-spiro[cyclobutane-1,1'-[2,6]naphthyridine]-3',5'-dione;

5-[(2-methylpropyl)aminocarbonyl]-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione, and diastereomers and enantiomers thereof;

5-(tert-butylaminocarbonyl)-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione, and diastereomers and enantiomers thereof;

5-[(2-pyridylmethyl)aminocarbonyl]-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione, and diastereomers and enantiomers thereof

5-(pyrimidin-2-yl)-2-(4-fluorobenzyl)-8-hydroxy-6-methyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione, and diastereomers and enantiomers thereof;

2-(3-chloro-4-fluorobenzyl)-8-hydroxy-6-cyclopropyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione;

(+)-2-(3-chloro-4-fluorobenzyl)-8-hydroxy-6-cyclopropyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione; and

(-)-2-(3-chloro-4-fluorobenzyl)-8-hydroxy-6-cyclopropyl-2,3,4,4a,5,6-hexahydro-2,6-naphthyridine-1,7-dione.

12. (currently amended) A pharmaceutical composition comprising an effective amount of a compound according to claim 1, ~~any one of claims 1 to 11~~, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

13. (currently amended) A method of inhibiting HIV integrase in a subject in need thereof which comprises administering to the subject an effective amount of the compound according to claim 1, ~~any one of claims 1 to 11~~, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof.

14. (currently amended) A method for preventing or treating infection by HIV or for preventing, treating or delaying the onset of AIDS in a subject in need thereof which comprises administering to the subject an effective amount of the compound according to claim 1, ~~any one of claims 1 to 11~~, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof.

15. (canceled)

16. (canceled)

17. (canceled)

18. (canceled)

19. (currently amended) A pharmaceutical combination which is (i) a compound according to claim 1, ~~any one of claims 1 to 11~~, or an individual enantiomer or diastereomer thereof, or a pharmaceutically acceptable salt thereof, and (ii) an HIV infection/AIDS antiviral agent selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors and nucleoside HIV reverse transcriptase inhibitors; wherein the compound of (i) or its pharmaceutically acceptable salt and the HIV infection/AIDS antiviral agent of (ii) are each employed in an amount that renders the combination effective for inhibiting HIV integrase, for preventing or treating infection by HIV, or for preventing, treating or delaying the onset of AIDS.

REMARKS

The status of the claims is as follows:

Original:	2-11
Currently amended:	1, 12-14 and 19
Canceled:	15-18
New:	None

With entry of this amendment, claims 1-14 and 19 are pending.

The sentence appearing on page 1 of the specification after the title and describing the status of the application has been updated.

The phrase "optical isomer" has been removed from claim 1 to remove the redundancy with "enantiomer or diastereomer".

The multiple dependency has been removed from claims 12-14 and 19, and use claims 15-18 have been canceled.

None of the foregoing revisions introduces new matter.

Respectfully submitted,

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